

10/068,398

(FILE 'HOME' ENTERED AT 10:57:29 ON 10 MAR 2003)

FILE 'CAPLUS' ENTERED AT 10:57:40 ON 10 MAR 2003

	E BALDRIDGE JORY/IN,AU
L1	12 S E3-6
	E JOHNSON DAVID A/IN,AU
L2	459 S E2-15
	E CLUFF CHRISTOPHER/IN,AU
L3	15 S E2-8
	E CLUFF CHRIS/IN,AU
L4	2 S E2
L5	479 S L1 OR L2 OR L3 OR L4
L6	1338 S AGP
L7	11 S AMINOALKYL GLUCOSAMINIDE
L8	25260 S LPS
L9	4476 S LIPID A
L10	29472 S L6 OR L7 OR L8 OR L9
L11	21 S L10 AND L5

=> d ibib ab 1-21

L11 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:90796 CAPLUS

TITLE: Immunostimulatory activity of aminoalkyl
glucosaminide 4-phosphates (AGPs):
Induction of protective innate immune responses by
RC-524 and RC-529

AUTHOR(S): Baldrige, Jory R.; Cluff, Christopher
W.; Evans, Jay T.; Lacy, Michael J.; Stephens,
Jeffrey R.; Brookshire, Valerie G.; Wang, Rong; Ward,
Jon R.; Yorgensen, Yvonne M.; Persing, David H.;
Johnson, David A.

CORPORATE SOURCE: Corixa Corporation, Hamilton, MT, 59840, USA

SOURCE: Journal of Endotoxin Research (2002), 8(6), 453-458

CODEN: JENREB; ISSN: 0968-0519

PUBLISHER: Maney Publishing

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Earlier we showed that the structural requirements for adjuvanticity among the aminoalkyl glucosaminide 4-phosphate (AGP) class of synthetic immunostimulants may be less strict than those for other endotoxic activities, including the induction of nitric oxide synthase in murine macrophages and cytokine prodn. in human whole blood. The known role of nitric oxide and pro-inflammatory cytokines in the activation of host defenses against infection prompted us to examine the ability of certain AGPs to enhance non-specific resistance in mice to *Listeria monocytogenes* and influenza infections as well as to stimulate the prodn. of pro-inflammatory cytokines in mouse splenocytes, human PBMCs, and human U937 histiocytic lymphoma cells. Intranasal administration of RC-524 or RC-529 to mice 2 days prior to a lethal influenza challenge provided significant protection in each case. Similarly, the i.v. administration of these AGPs induced resistance to *L. monocytogenes* infection as measured by survival or redn. of bacteria in the spleen. Activation of the innate immune response by AGPs appears to involve activation of Toll-like receptor 4 (TLR4) because RC-524 failed to elicit a protective effect in C3H/HeJ mice which have a defect in TLR4 signaling or induce significant cytokine levels in C3H/HeJ splenocytes. Both AGPs also stimulated pro-inflammatory cytokine release in human cell cultures in a dose-dependent manner.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:759775 CAPLUS

DOCUMENT NUMBER: 137:261484

TITLE: Taking toll: lipid A mimetics as
adjuvants and immunomodulators

AUTHOR(S): Persing, David H.; Coler, Rhea N.; Lacy, Michael J.;
Johnson, David A.; Baldrige, Jory R.
; Hershberg, Robert M.; Reed, Steven G.

CORPORATE SOURCE: Corixa, Seattle, WA, 98104, USA

SOURCE: Trends in Microbiology (2002), 10(10, Suppl.), s32-s37

CODEN: TRMIEA; ISSN: 0966-842X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Vaccine adjuvants based on the structure of lipid A, such as monophosphoryl lipid A (MLA), have proven to be safe and effective in inducing immune responses to heterologous proteins in animal and human vaccines. Recent work on the development of a recombinant vaccine for leishmaniasis has demonstrated that a clin. grade MLA formulation - MPL adjuvant - is essential in the development of a protective response. Preliminary evidence suggests that MLA and a chem. distinct family of lipid A mimetics - the aminoalkyl glucosaminide 4-phosphates - act on Toll-like receptor 4 (TLR4). As TLR4 agonists, they have potent immunomodulatory effects when used both as vaccine adjuvants and as stand-alone products. Novel approaches to vaccine development could benefit from taking full advantage of the effects of these compds. on innate and adaptive responses. Vaccine adjuvants based on the structure of lipid A have proven to be safe and effective in inducing immune responses to heterologous proteins in animal and human vaccines. Novel approaches to vaccine development could benefit from taking full advantage of the effects of these compds. on innate and adaptive responses.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002:123023 CAPLUS
 DOCUMENT NUMBER: 136:182448
 TITLE: Aminoalkyl glycosaminide phosphate adjuvants
 INVENTOR(S): Johnson, David A.; Baldridge, Jory; Sowell, Greg
 PATENT ASSIGNEE(S): Corixa Corporation, USA
 SOURCE: PCT Int. Appl., 47 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012258	A1	20020214	WO 2001-US24284	20010803
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001081001	A5	20020218	AU 2001-81001	20010803
PRIORITY APPLN. INFO.: US 2000-223056P P 20000804				
WO 2001-US24284 W 20010803				
AB The authors disclose the prepn., pyrogenicity, and immunostimulatory activity of a 2-deoxy-2-amino-.beta.-D-glucopyranose (glucosamine) glycosidically linked to a cyclic aminoalkyl (aglycon) group. An illustrative compd., RC-533, was shown to enhance both antibody and cytotoxic T-cell response to the surface antigen of hepatitis B virus.				
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT				

L11 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:868475 CAPLUS
 DOCUMENT NUMBER: 136:628
 TITLE: Prophylactic and therapeutic treatment of infectious and other diseases with mono- and disaccharide-based compounds
 INVENTOR(S): Persing, David H.; Crane, Richard Thomas; Elliot, Gary T.; Ulrich, J. Terry; Lacy, Michael J.; Johnson, David A.; Baldridge, Jory R.; Wang, Rong
 PATENT ASSIGNEE(S): Corixa Corporation, USA
 SOURCE: PCT Int. Appl., 57 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001090129	A2	20011129	WO 2001-US16327	20010518
WO 2001090129	A3	20020606		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002077304	A1	20020620	US 2001-861466	20010518
EP 1284740	A2	20030226	EP 2001-948222	20010518
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.: US 2000-205820P P 20000519				
US 2001-281567P P 20010404				
WO 2001-US16327 W 20010518				
OTHER SOURCE(S): MARPAT 136:628				

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AB Methods and compns. for treating or ameliorating diseases and other conditions, such as infectious diseases, autoimmune diseases and allergies are provided. The methods employ mono- and disaccharide-based compds. for selectively stimulating immune responses in animals and plants.

L11 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:757768 CAPLUS

DOCUMENT NUMBER: 135:302901

TITLE: Aminoalkyl glucosaminide phosphate compounds and their use as adjuvants and immunoeffectors

INVENTOR(S): Johnson, David A.; Sowell, C. Gregory

PATENT ASSIGNEE(S): Corixa Corporation, USA

SOURCE: U.S., 44 pp., Cont.-in-part of U.S. 6,113,918.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6303347	B1	20011016	US 1999-439839	19991112
US 6113918	A	20000905	US 1997-853826	19970508
WO 2001034617	A2	20010517	WO 2000-US31340	20001113
WO 2001034617	A3	20011108		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 2001019189	A5	20010606	AU 2001-19189	20001113
EP 1230250	A2	20020814	EP 2000-982119	20001113
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
US 2002045586	A1	20020418	US 2001-808669	20010314
US 2002048588	A1	20020425	US 2001-905160	20010712
NO 2002002207	A	20020710	NO 2002-2207	20020508
PRIORITY APPLN. INFO.:			US 1997-853826	A2 19970508
			US 1991-815250	A 19911231
			US 1998-138305	A1 19980821
			US 1999-429238	A 19991028
			US 1999-439839	A 19991112
			US 1999-439849	B1 19991112
			US 2000-190444P	P 20000317
			WO 2000-US31340	W 20001113

OTHER SOURCE(S): MARPAT 135:302901

AB Aminoalkyl glucosaminide phosphate (AGP) compds. that are adjuvants and immunoeffectors are described and claimed. The compds. have a 2-deoxy-2-amino glucose in glycosidic linkage with an aminoalkyl (aglycon) group. Compds. are phosphorylated at the 4 or 6 carbon on the glucosaminide ring and comprise three 3-alkanoyloxyalkanoyl residues. The compds. augment antibody prodn. in immunized animals as well as stimulate cytokine prodn. and activate macrophages. Methods for using the compds. as adjuvants and immunoeffectors are also disclosed.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:713123 CAPLUS

DOCUMENT NUMBER: 135:267269

TITLE: Mono- and disaccharides for the treatment of nitric oxide related disorders

INVENTOR(S): Elliot, Gary; Johnson, David; Weber, Patricia A.; Sowell, Greg

PATENT ASSIGNEE(S): Corixa Corp., USA

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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 WO 2001070209 A2 20010927 WO 2001-US8513 20010315
 WO 2001070209 A3 20020418
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
 HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
 LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
 RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
 VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 EP 1265620 A2 20021218 EP 2001-920455 20010315
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 PRIORITY APPLN. INFO.: US 2000-190444P P 20000317
 WO 2001-US8513 W 20010315
 OTHER SOURCE(S): MARPAT 135:267269
 AB Methods for treating diseases or conditions modulated or ameliorated by
 nitric oxide, particularly ischemia and reperfusion injury, are provided,
 using glycolipids structurally related to monophosphoryl lipid
 A but with notable redn. in proinflammatory and pyrogenic
 activity.

L11 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:525947 CAPLUS
 DOCUMENT NUMBER: 135:112005
 TITLE: Composition of antigen and glycolipid adjuvant
 sublingual administration
 INVENTOR(S): Wheeler, Alan; Elliott, Garry; Cluff, Christopher
 Wallace
 PATENT ASSIGNEE(S): Allergy Therapeutics Limited, UK; Corixa Corporation
 SOURCE: PCT Int. Appl., 55 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001051082	A1	20010719	WO 2001-GB142	20010115
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
GB 2360210	A1	20010919	GB 2001-1035	20010115
EP 1255563	A1	20021113	EP 2001-942305	20010115
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PRIORITY APPLN. INFO.:			GB 2000-891 A 20000114 WO 2001-GB142 W 20010115	

AB A method of producing a mucosal and systemic immune response in a mammal
 comprising administering sublingually an effective amt. of a compn.
 comprising at least one antigen and a glycolipid adjuvant to said mammal.
 An example is given for prepn. of MPL (a form of 3 de-O-acylated
 monophosphoryl lipid A) adjuvant with DPPC.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:360008 CAPLUS
 DOCUMENT NUMBER: 134:353474
 TITLE: Preparation of aminoalkyl
 glucosaminide phosphates and their use as
 adjuvants and immuno-effectors
 INVENTOR(S): Johnson, David A.; Sowell, C. Gregory
 PATENT ASSIGNEE(S): Corixa Corporation, USA
 SOURCE: PCT Int. Appl., 147 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034617	A2	20010517	WO 2000-US31340	20001113
WO 2001034617	A3	20011108		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6303347	B1	20011016	US 1999-439839	19991112
AU 2001019189	A5	20010606	AU 2001-19189	20001113
EP 1230250	A2	20020814	EP 2000-982119	20001113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2002002207	A	20020710	NO 2002-2207	20020508
PRIORITY APPLN. INFO.:			US 1999-439839	A 19991112
			US 1997-853826	A2 19970508
			WO 2000-US31340	W 20001113

OTHER SOURCE(S): MARPAT 134:353474

AB Aminoalkyl glucosaminide phosphate compds. (AGP) I were prep'd. wherein, X is selected from the group consisting of O and S at the axial or equatorial position; Y is selected from the group consisting of O and NH; Q is (CH₂)_n; L is (CH₂)_m; W is (CH₂)_q; n, m, p, q are integers from 0 to 6; R is (CH₂)₁₀Me; R1-R3 are the same or different and are normal fatty acyl residues having from 1 to about 20 carbon atoms and where one of R1-R3 is optionally hydrogen; R4 and R5 are the same or different and are selected from the group consisting of H and methyl; R6 and R7 are the same or different and are selected from the group consisting of H, hydroxy, alkoxy, phosphono, phosphonoxy, sulfo, sulfoxy, amino, mercapto, cyano, nitro, formyl and carboxy, and esters and amides thereof; and R8 and R9 are the same or different and are selected from the group consisting of phosphono and H, and at least one of R8 and R9 is phosphono, that are adjuvants and immuno-effectors are described and claimed. The compds. have a 2-deoxy-2-amino glucose in glycosidic linkage with an aminoalkyl (aglycon) group. Compds. are phosphorylated at the 4 or 6 carbon on the glucosaminide ring and comprise three 3-alkanoyloxyalkanoyl residues. The compds. augment antibody prodn. in immunized animals as well as stimulate cytokine prodn. and activate macrophages. Methods for using the compds. as adjuvants and immuno-effectors are also disclosed. Thus, N-[(R)-3-hydroxytetradecanoyl]-O-[2-deoxy-4-O-phosphono-2-[(R)-3-dodecanoyloxytetradecanoylamino]-3-O-[(R)-3-tetradecanoyloxytetradecanoyl]-.alpha.-L-D-glucopyranosyl]-L-serine triethylammonium salt was prep'd. and tested in mice as adjuvants and immuno-effectors. Mice vaccinated with formalin-inactivated influenza and the AGP compds. of the subject invention mounted a protective immune response to an influenza challenge as well as produced antibody to that antigen.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:407550 CAPLUS

DOCUMENT NUMBER: 134:36798

TITLE: Monophosphoryl lipid A enhances mucosal and systemic immunity to vaccine antigens following intranasal administration

AUTHOR(S): Baldridge, Jory R.; Yorgensen, Yvonne; Ward, Jon R.; Ulrich, J. Terry

CORPORATE SOURCE: Ribic ImmunoChem Research Inc., Hamilton, MT, 59840, USA

SOURCE: Vaccine (2000), 18(22), 2416-2425

CODEN: VACCDE; ISSN: 0264-410X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The induction of protective immunity stemming from vaccines delivered by mucosal routes is dependent on the development of safe and effective mucosal adjuvants. The immunostimulant monophosphoryl lipid A (MPL) was evaluated for its ability to enhance both systemic and mucosal immunity to three distinct antigens. Vaccines formulated with MPL and hepatitis B surface antigen, tetanus toxoid or influenza antigens were administered by intranasal delivery to mice. In each case the vaccines

formulated with MPL resulted in enhanced IgA titers from mucosal samples. Enhanced IgA concns. were detected in samples from both local and distal mucosal sites. In addn., the MPL formulated vaccines induced systemic immunity characteristic of a Th1-type of response. Serum IgG2a antibody titers were elevated and cytotoxic T cell activity was enhanced.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:769093 CAPLUS

DOCUMENT NUMBER: 132:137639

TITLE: Synthesis and biological evaluation of a new class of vaccine adjuvants: aminoalkyl glucosaminide 4-phosphates (AGPs).
[Erratum to document cited in CA131:272113]

AUTHOR(S): Johnson, David A.; Sowell, C. Gregory; Johnson, Craig L.; Livesay, Mark T.; Keegan, David S.; Gustafson, Gary L.; Rhodes, Michael J.; Ulrich, J. Terry; Ward, Jon R.; Cantrell, John L.; Brookshire, Valerie G.

CORPORATE SOURCE: Pharmaceutical Discovery Division, Ribic ImmunoChem Research, Inc., Hamilton, MT, 59840, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(22), 3260
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The name of coauthor Gary L. Gustafson was omitted fro the list of authors' names; the complete list is reprinted.

L11 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:664948 CAPLUS

DOCUMENT NUMBER: 132:26772

TITLE: Monophosphoryl Lipid A (MPL)
Formulations for the Next Generation of Vaccines

AUTHOR(S): Baldridge, Jory R.; Crane, R. Thomas

CORPORATE SOURCE: Ribic ImmunoChem Research, Inc., Hamilton, MT, 59840, USA

SOURCE: Methods (Orlando, Florida) (1999), 19(1), 103-107

CODEN: MTHDE9; ISSN: 1046-2023

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Many of the latest trends in vaccine development are dependent on immunol. adjuvants that mediate and promote a wide variety of immune responses. One promising adjuvant candidate, monophosphoryl lipid A (MPL) immunostimulant, is being investigated with many of these new vaccine approaches in either preclin. or clin. trials. This is possible because different vehicle formulations can significantly influence the type of immunol. response MPL promotes. Procedures are provided for formulating MPL in an aq. vehicle or an oil-in-water emulsion. These two MPL formulations can be beneficial for most vaccine approaches being investigated today. (c) 1999 Academic Press.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:663073 CAPLUS

DOCUMENT NUMBER: 132:23151

TITLE: 3-O-Desacyl Monophosphoryl Lipid A
Derivatives: Synthesis and Immunostimulant Activities

AUTHOR(S): Johnson, David A.; Keegan, David S.; Sowell, C. Gregory; Livesay, Mark T.; Johnson, Craig L.; Taubner, Lara M.; Harris, Annalivia; Myers, Kent R.; Thompson, Jennifer D.; Gustafson, Gary L.; Rhodes, Michael J.; Ulrich, J. Terry; Ward, Jon R.; Yorgensen, Yvonne M.; Cantrell, John L.; Brookshire, Valerie G.

CORPORATE SOURCE: Pharmaceutical Discovery Division, Ribic ImmunoChem Research Inc., Hamilton, MT, 59840, USA

SOURCE: Journal of Medicinal Chemistry (1999), 42(22), 4640-4649

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The synthesis of a series of novel analogs of lipid A, the active principle of lipopolysaccharide, is reported. In these

compds., the 1-O-phosphono and (R)-3-hydroxytetradecanoyl moieties of native *Salmonella minnesota* R595 lipid A have been replaced with hydrogen and the length of the normal fatty acyl residues has been systematically varied. Normal fatty acid chain length in the 3-O-desacyl monophosphoryl lipid A (MLA) series is shown to be a crit. determinant of iNOS gene expression in activated mouse macrophages and the induction of pro-inflammatory cytokines in human peripheral monocytes. Examn. of pyrogenicity in rabbits and lethal toxicity in D-galactosamine-treated mice shows that toxic effects in the MLA series can be ameliorated by modifying fatty acid chain length. When used as an adjuvant for tetanus toxoid vaccines, certain MLA derivs. enhance the prodn. of tetanus toxoid-specific antibodies in mice.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:536699 CAPLUS

DOCUMENT NUMBER: 131:272113

TITLE: Synthesis and biological evaluation of a new class of vaccine adjuvants: aminoalkyl glucosaminide 4-phosphates (AGPs)

AUTHOR(S): Johnson, David A.; Sowell, C. Gregory; Johnson, Craig L.; Livesay, Mark T.; Keegan, David S.; Rhodes, Michael J.; Ulrich, J. Terry; Ward, Jon R.; Cantrell, John L.; Brookshire, Valerie G.

CORPORATE SOURCE: Pharmaceutical Discovery Division, Ribi ImmunoChem Research, Inc., Hamilton, MT, 59840, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(15), 2273-2278

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A novel series of acylated .omega.-aminoalkyl 2-amino-2-deoxy-4-phosphono-.beta.-D-glucopyranosides (aminoalkyl glucosaminide 4-phosphates) was synthesized and screened for immunostimulant activity. Several of these compds. enhance the prodn. of tetanus toxoid-specific antibodies in mice and augment vaccine-induced cytotoxic T cells against EG.7-ova target cells.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:796363 CAPLUS

DOCUMENT NUMBER: 130:139549

TITLE: Chemical synthesis of the major constituents of *Salmonella minnesota* monophosphoryl lipid A

AUTHOR(S): Johnson, David A.; Sowell, C. Gregory; Keegan, David S.; Livesay, Mark T.

CORPORATE SOURCE: Pharmaceutical Discovery Division, Ribi ImmunoChem Research, Inc., Hamilton, MT, 59840, USA

SOURCE: Journal of Carbohydrate Chemistry (1998), 17(9), 1421-1426

CODEN: JCACDM; ISSN: 0732-8303

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two aminodeoxy glycopospholipids major constituents of *Salmonella minnesota* were prepd. via coupling of lipids with sugars.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:508532 CAPLUS

DOCUMENT NUMBER: 129:225496

TITLE: Antiischemic effect of monophosphoryl lipid A in conscious rabbits with hypercholesterolemia and atherosclerosis

AUTHOR(S): Szilvassy, Zoltan; Ferdinandy, Peter; Cluff, Christopher W.; Elliott, Gary T.

CORPORATE SOURCE: First Department of Medicine, Albert Szent-Gyorgyi Medical University, Szeged, Hung.

SOURCE: Journal of Cardiovascular Pharmacology (1998), 32(2), 206-212

CODEN: JCPCDT; ISSN: 0160-2446

PUBLISHER: Lippincott-Raven Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors studied whether monophosphoryl lipid A (MLA), an endotoxin deriv., protected the heart from planned ischemia in hypercholesterolemic conscious rabbits. Normal and hypercholesterolemic (8-wk exposure to 1.5% cholesterol-enriched diet) conscious rabbits with right ventricular electrode and left ventricular polyethylene catheters were subjected to ventricular overdrive pacing (VOP; 500 beats/min over 10 min = control VOP). The resulting intracavitary ST-segment elevation, increase in left ventricular end-diastolic pressure (LVEDP), and a redn. of ventricular effective refractory period (VERP) were measured. Three days later the animals were given a single i.v. bolus of 10 or 30 .mu.g/kg MLA or its solvent or both, and a second VOP (test VOP) was applied 24 h later. MLA decreased ST elevation and LVEDP increase from 2.1 .+- 0.16 to 1.27 .+- 0.25 and 0.97 .+- 0.13 mV and 14.6 .+- 1.2 to 11.1 .+- 1.0 and 12.4 .+- 1.2 mm Hg in normal animals and from 2.55 .+- 0.14 to 1.31 .+- 0.12 and 0.96 .+- 0.30 mV and from 21.0 .+- 1.6 to 11.7 .+- 1.3 and 12.4 .+- 1.3 mm Hg in atherosclerotic animals after 10- and 30-.mu.g/kg doses, resp. (p < 0.001 for each). VOP-induced VERP redn. was also significantly alleviated by both MLA doses; nevertheless, 30-.mu.g/kg MLA significantly prolonged resting VERP with a slight VERP redn. in response to pacing in both normal and atherosclerotic animals. The authors conclude that MLA produces a delayed antiischemic effect in both normal and hypercholesterolemic/atherosclerotic conscious rabbits.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:302174 CAPLUS

DOCUMENT NUMBER: 126:342189

TITLE: Effective adjuvants for the induction of antigen-specific delayed-type hypersensitivity

AUTHOR(S): Baldridge, Jory R.; Ward, Jon R.

CORPORATE SOURCE: Ribic ImmunoChem Research, Inc., Hamilton, MT, 59840, USA

SOURCE: Vaccine (1997), 15(4), 395-401

CODEN: VACCDE; ISSN: 0264-410X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Vaccines utilizing poorly immunogenic subunit antigens are dependent upon adjuvants to drive the appropriate T cell responses. In an effort to det. the ability of several adjuvants to promote cell-mediated immunity (CMI), we assessed delayed-type hypersensitivity (DTH) in mice inoculated with heat-killed *Listeria monocytogenes* (HKLM) vaccines. The vaccines were formulated as oil-in-water emulsions contg. one or more of the following bacterial-derived immunostimulators: MPL immunostimulant, a monophosphoryl lipid A prepn., synthetic trehalose dicorynomycolate (TDCM) and *Mycobacterium phlei* cell wall skeleton (CWS). Oil-in-water emulsions contg. HKLM without adjuvants did not induce DTH responsiveness in mice. The incorporation of TDCM, or MPL plus TDCM and/or CWS to the formulation enabled the HKLM vaccine to stimulate CMI characterized by DTH responsiveness. Following antigen challenge the resulting increases in footpad thickness ranged from 15-20% and were comparable to the DTH driven by complete Freund's adjuvant. Adjuvants composed of MPL/TDCM and MPL/TDCM/CWS induced responses equiv. to those measured in mice immunized with viable *L. monocytogenes*, and the responses remained at these levels for at least 2 mo. Furthermore, in vivo depletion of CD4+ T cells, but not CD8+ T cells, abrogated the induction and expression of DTH, indicating that the response is mediated by CD4+ T cells.

L11 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:763224 CAPLUS

DOCUMENT NUMBER: 126:131266

TITLE: Efficient asymmetric synthesis of (R)-3-hydroxy- and alkanoyloxytetradecanoic acids and method for the determination of enantiomeric purity

AUTHOR(S): Keegan, David S.; Hagen, Steven R.; Johnson, David A.

CORPORATE SOURCE: Pharmaceutical Discovery Div., Ribic ImmunoChem Res., Inc., MT, 59840, USA

SOURCE: Tetrahedron: Asymmetry (1996), 7(12), 3559-3564

CODEN: TASYE3; ISSN: 0957-4166

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An efficient synthesis of the (R)-3-hydroxy- and alkanoyloxytetradecanoic acid components of bacterial lipid A has been achieved using a Ru(II)-Binap-catalyzed low-pressure hydrogenation of

Me(CH₂)₁₀COCH₂CO₂Me. The enantiomeric purity of(R)-
Me(CH₂)₁₀CH(OH)OCH₂CO₂CH₂COC₆H₄Br-4 could be assessed directly by chiral
HPLC, obviating sep. derivatization steps and/or chiral NMR shift studies.

L11 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:412265 CAPLUS
TITLE: Synthesis and immunostimulant activities of
monophosphoryl lipid A derivatives
AUTHOR(S): Johnson, David A.; Keegan, David S.; Sowell,
C. Gregory; Livesay, Mark T.; Cantrell, John L.;
Ulrich, J. Terry
CORPORATE SOURCE: Pharmaceutical Discovery Division, Ribl ImmunoChem
Research, Inc., Hamilton, MT, 59840, USA
SOURCE: Book of Abstracts, 212th ACS National Meeting,
Orlando, FL, August 25-29 (1996), CARB-037. American
Chemical Society: Washington, D. C.
CODEN: 63BFAF
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB In addn. to their capacity to induce toxic reactions such as fever and
lethal shock, bacterial lipopolysaccharide (LPS) and its
endotoxic principle lipid A can have beneficial
effects including the enhancement of non-specific immune responses against
tumor cells and microbial pathogens. As part of a program aimed at
developing synthetic immunostimulants possessing a better balance between
beneficial and endotoxic effects, we have prepd. synthetic subunit analogs
of S. minnesota lipid A. Synthetic methodol. for the
efficient construction of the 3-O-desacyl monophosphoryl lipid
A deriv. shown and related compds. will be presented together with
a discussion of their antitumor effects.

L11 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:317763 CAPLUS
DOCUMENT NUMBER: 122:103470
TITLE: Soluble CD14 truncated at amino acid 152 binds
lipopolysaccharide (LPS) and enables
cellular response to LPS
AUTHOR(S): Juan, Todd S.-C.; Kelley, Michael J.; Johnson,
David A.; Busse, Leigh A.; Hailman, Eric; Wright,
Samuel D.; Lichenstein, Henri S.
CORPORATE SOURCE: Amgen Inc., Thousand Oaks, CA, 91320, USA
SOURCE: Journal of Biological Chemistry (1995), 270(3), 1382-7
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular
Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB CD14 is a 55-kDa glycoprotein which binds lipopolysaccharide (LPS
) and enables LPS-dependent responses in a variety of cells. To
identify the domains in CD14 required for function, the authors deleted
increasing amts. of CD14 from the C-terminus. Truncated CD14 cDNA
sequences were transfected into COS-7 cells and serum-free conditioned
medium was analyzed for mutant CD14 expression and bioactivity. Mutant
CD14s contg. as few as 152 amino acids were found to have activity equiv.
t.omega. full length sCD14. To further characterize the mutant CD14, the
authors constructed a stable Chinese hamster ovary cell line expressing
sCD141-152 and purified the protein to homogeneity. The sCD141-152 bound
radioactive LPS, enabled U373 cells to synthesize interleukin 6
in response to LPS, and enabled human neutrophils to respond to
smooth LPS. In all of these assays, the behavior of sCD141-152
was quant. similar to full-length sCD14. The authors also found that two
neutralizing anti-CD14 antibodies (3C10 and MEM-18) bound and neutralized
sCD141-152. The authors conclude from these expts. that the N-terminal
152 amino acids of CD14 are sufficient to bind LPS and confer
essentially wild-type bioactivity in vitro.

L11 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1994:74995 CAPLUS
DOCUMENT NUMBER: 120:74995
TITLE: Lipopolysaccharide (LPS)-binding protein
accelerates the binding of LPS to CD14
AUTHOR(S): Hailman, Eric; Lichenstein, Henri S.; Wurfel, Mark M.;
Miller, David S.; Johnson, David A.; Kelley,
Michael; Busse, Leigh A.; Zukowski, Mark M.; Wright,
Samuel D.
CORPORATE SOURCE: Lab. Cell. Physiol. Immunol., Rockefeller Univ., New
York, NY, 10021, USA
SOURCE: Journal of Experimental Medicine (1994), 179(1),

269-77

CODEN: JEMEAV; ISSN: 0022-1007

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB CD14 is a 55-kD protein found as a glycosylphosphatidylinositol (GPI)-anchored protein on the surface of monocytes, macrophages, and polymorphonuclear leukocytes, and as a sol. protein in the blood. Both forms of CD14 participate in the serum-dependent responses of cells to bacterial lipopolysaccharide (LPS). While CD14 has been described as a receptor for complexes of LPS with LPS-binding protein (LBP), there has been no direct evidence showing whether a ternary complex of LPS, LBP, and CD14 is formed, or whether CD14 binds LPS directly. Using nondenaturing polyacrylamide gel electrophoresis (native PAGE), the authors show that recombinant sol. CD14 (rsCD14) binds LPS in the absence of LBP or other proteins. Binding of LPS to CD14 is stable and of low stoichiometry (one or two mols. of LPS per rsCD14). Recombinant LBP (rLBP) does not form detectable ternary complexes with rsCD14 and LPS, but it does accelerate the binding of LPS to rsCD14. The rLBP facilitates the interaction of LPS with rsCD14 at substoichiometric concns., suggesting that LBP functions catalytically, as a lipid transfer protein. Complexes of LPS and rsCD14 formed in the absence of LBP or other serum proteins strongly stimulate integrin function on PMN and expression of E-selectin on endothelial cells, demonstrating that LBP is not necessary for CD14-dependent stimulation of cells. Apparently, CD14 acts as a sol. and cell surface receptor for LPS, and LBP may function primarily to accelerate the binding of LPS to CD14.

L11 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1987:437707 CAPLUS

DOCUMENT NUMBER:

107:37707

TITLE:

An early response to lipopolysaccharide is the elicitation of macrophages specialized for antigen degradation with negative regulatory effects on the induction of specific immune responses

AUTHOR(S):

Cluff, Christopher W.; Ziegler, H. Kirk

CORPORATE SOURCE:

Sch. Med., Emory Univ., Atlanta, GA, 30322, USA

SOURCE:

Infection and Immunity (1987), 55(6), 1346-54

CODEN: INFIBR; ISSN: 0019-9567

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB The ability of macrophages to catabolize antigens is relevant both as a means to process complex antigens before presentation to T cells and as a way to down-regulate immune responses by destroying the antigenicity of polypeptides. With these considerations in mind, the authors investigated the regulation of macrophage catabolic activity by lipopolysaccharide (LPS). Catabolic activity was quantitated by following the distribution and mol. form of 125I-labeled surface components of heat-killed *Listeria monocytogenes* after their uptake by macrophages. The authors compared the catabolic activity of macrophages from peritoneal exudates of mice injected i.p. with saline or LPS and found that LPS-elicited macrophages displayed a greatly enhanced rate of catabolism. This increase in catabolic activity peaked 3 days after LPS injection and slowly declined thereafter, approaching a base-line level after 3 wk. The enhancement of catabolic activity was under Lps gene control. Macrophages that were elicited 3 days after i.p. injection of LPS rapidly destroyed the antigenicity of bacterial antigens, expressed low levels of Ia mols., and processed and presented antigen slowly when tested as antigen-presenting cells in vitro. An injection of LPS before infection with *L. monocytogenes* resulted in diminished development of T-cell reactivity to this organism. Apparently, LPS elicits a macrophage population specialized for antigen degradn. functions, with neg. regulatory effects on the induction of specific immune responses.